Navigating uncertainty in pharmaceutical manufacturing: The critical role of technology transfer

The pharmaceutical manufacturing landscape is in a period of transition. Some of the changes reflect advances in science and technology that will bring innovative therapies to patients more quickly. Others arise from geopolitical tensions, regulatory changes, and unpredictable market shifts that contribute to a climate of uncertainty that can impact production, development timelines, and market stability.

In this changing environment, technology transfer is a pivotal navigational strategy, as it enables pharmaceutical companies to adapt quickly to changes in demand, regulatory policies, or market dynamics. Efficient technology transfer helps maintain product quality, protect intellectual property, manage costs, and scale operations, thereby ensuring that companies can respond effectively to new opportunities or challenges, maintain competitive advantage, and ensure uninterrupted supply of medications to patients. "The goal of technology transfer activities is to transfer product and process knowledge between development and manufacturing, and within or between manufacturing sites to achieve product realization. This knowledge forms the basis for the manufacturing process, control strategy, process validation approach, and ongoing continual improvement."

ICH Q10 Guidance for Industry





Understanding technology transfer and its significance

Technology transfer is the systematic movement of scientific methods and manufacturing processes from development to production or between sites, ensuring product consistency, quality, and regulatory compliance. This process is critical for producing pharmaceuticals safely and cost-effectively across various locations and scales, maintaining project timelines, and facilitating the seamless scale-up of new drugs and therapies. It ensures that innovative treatments reach patients promptly. Necessary during transitions such as scaling from clinical to commercial volumes, optimizing capacity between sites, or changing between CDMO partners, technology transfer demands detailed planning, comprehensive documentation, and rigorous validation to meet original product specifications and quality attributes.

Enhancing supply chain resilience

Effective technology transfer also plays a vital role in enhancing supply chain resilience by ensuring the robust sourcing of raw materials and packaging components. It supports detailed vendor management, crucial for maintaining quality across global supply networks. In logistics, the transfer of manufacturing processes includes critical shipping protocols and optimized route planning to ensure that clinical trial materials and finished products are delivered under the right conditions, preserving their integrity and efficacy. These aspects are crucial for adapting to the fast-paced and often unpredictable pharmaceutical market, ensuring that operations remain agile and responsive to any shifts in demand or regulatory changes.



Tech transfer challenges: Considerations for OSDs, biologics, and advanced therapies

Oral solid dosage (OSD), biological, and cell and gene therapy products each present unique challenges in technology transfer. For small molecule OSDs, the primary challenges revolve around achieving consistent batch reproducibility and maintaining formulation stability, particularly when active pharmaceutical ingredients (APIs) are sensitive to environmental variables like humidity and temperature. Critical factors include the precise replication of process parameters that influence physical properties of the tablets or capsules, such as hardness and dissolution rate. Additionally, ensuring the uniformity of particle size distribution during milling or granulation is essential, as it directly affects the compaction and dissolution profile of the final product. In multipurpose facilities, stringent controls are required to prevent cross-contamination between products, necessitating thorough cleaning and validation processes.

With respect to <u>biologics</u>, the manufacture of these products involves complex biological processes that are sensitive to slight changes in process conditions. A key technical hurdle is the control of the bioreactor environment during scale-up, which can drastically affect the quality of the product. Scaling up cell culture processes while maintaining the integrity and functionality of proteins, which can be affected by changes in pH, temperature, or oxygen levels, requires meticulous control over bioreactor conditions, as well as rigorous optimization of media and feed strategies to ensure consistent quality and yield throughout the production scale.

The robustness of the purification steps must also be ensured to prevent the loss of yield and product purity. Additionally, biologics are susceptible to variations in post-translational modifications, which can impact the efficacy and safety of the final product. The purification process also needs to be finely tuned to ensure product purity and yield, which can be particularly challenging during scale-up.

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The complexities of tech transfer extend into the domain of <u>cell and gene therapies (CGTs</u>), where the challenges are uniquely stringent due to the nature of the products involved. These therapies demand an exceptionally high degree of precision in process replication, with strict controls over environmental variables to maintain the viability and functionality of live biological materials. Equipment and facility differences necessitate careful calibration and compatibility checks, and maintaining high standards of quality control and training for new personnel are vital. The scale-up from research and development to commercial production must not only preserve the therapeutic qualities but also ensure the consistent quality and efficacy of larger production volumes.

Assessing the quality and potency of CGTs requires robust analytical methods. As processes are transferred to different manufacturing sites, these methods must be carefully adapted and validated to ensure they remain effective. Moreover, tech transfer for CGTs poses additional challenges due to their unique and complex manufacturing processes that often lack the standardization seen in more traditional biologics. Effective communication and detailed documentation are crucial for smooth coordination between teams, while managing the supply chain involves ensuring the availability and quality of materials and handling logistics efficiently. Protecting intellectual property and maintaining confidentiality throughout the process are essential. Effectively addressing these challenges is vital for safeguarding the integrity of CGTs as they reach patients.

Ensuring regulatory compliance

OSD, biological, and CGTs must adhere to rigorous regulatory standards set by authorities such as the FDA and EMA. This involves detailed documentation of every aspect of the manufacturing process, from raw material sourcing to final product testing, to demonstrate compliance with Good Manufacturing Practices (GMP).

Maintaining regulatory compliance during the technology transfer process is essential for accelerating smooth market entry, safeguarding product quality and safety, and ensuring that the product remains consistent across different manufacturing sites, which is crucial for maintaining the trust of healthcare providers and patients. The key regulatory considerations are shown below.



Documentation and data Integrity.

Providing comprehensive and accurate documentation is essential for regulatory compliance. Regulators require detailed records of batch processing, quality control results, and validations to verify that the manufacturing process is controlled and consistent with approved standards.

Standardized procedures. Regulators mandate that products are manufactured under standardized conditions to guarantee consistent quality. Any deviations from these standardized procedures could lead to non-compliance, potentially resulting in product recalls or regulatory sanctions. Scale-up reliability. Scaling up manufacturing processes introduces increased risks of deviations, which can compromise product quality and safety. Regulatory compliance requires that the product, regardless of scale or manufacturing site, adheres to the same quality standards established for the originally approved product.

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Skilled and trained staff. Properly trained staff are critical for maintaining compliance. They must be well-versed in regulatory standards and capable of implementing these standards in their daily operations. Particularly for CGTs, where regulatory guidance is continually evolving, partnering with experts who are abreast of the latest changes is crucial. These experts can provide invaluable insights into strategic compliance planning and operational adjustments required to navigate the shifting regulatory requirements.

Validation and quality assurance. Extensive validation studies are required to prove that the process remains under control and produces a consistent product at different scales and locations. For OSD, this might include validation of the mixing and compression processes. For biologics, validation efforts focus on critical aspects like cell line authenticity, media preparation, and the efficiency of purification techniques. For CGTs, this might include additional considerations such as the validation of viral vector titration methods and cell viability assays.

The value of strategic partnerships in technology transfer

Strategic partnerships play a crucial role in successful technology transfers by helping to identify and mitigate process risks. A well-chosen strategic partner can preserve project timelines, overcome common technology transfer challenges, and lead to significant cost savings. This is particularly vital in a landscape where rapid adaptability can determine market success or failure. The following partnership considerations should be prioritized for a streamlined technology transfer.

Technological compatibility.

The technological alignment between the partnering companies ensures that the manufacturing processes and equipment are compatible, minimizing the need for extensive modifications. For example, a company specializing in aseptic filling should seek a CDMO partner with compatible sterile handling and packaging technologies to streamline the integration of new products into existing lines.

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Expertise. A CDMO's expertise in specific therapeutic areas or with certain drug modalities can drastically reduce the learning curve and associated risks in the technology transfer process. Partners with a proven track record in scaling up similar products can provide invaluable insights that prevent common pitfalls.

Regulatory strategy alignment. Aligning with a CDMO partner that has a strong regulatory strategy is crucial. This includes a thorough understanding of both current and emerging regulations in all intended markets. A partner well-versed in navigating complex regulatory landscapes can expedite product approval processes by ensuring compliance at every stage of development and transfer.

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Quality assurance capabilities. The quality assurance practices of the CDMO partner must meet or exceed the rigorous standards required in pharmaceutical manufacturing. This includes robust systems for monitoring and controlling quality throughout the production process, which is essential for maintaining the integrity and efficacy of the product.

Effective communication and project transparency.

Open and continuous communication channels between partners ensure that any issues are swiftly addressed and that the project remains on schedule. Transparency in operations and decision-making fosters trust and facilitates smoother project execution.

A strategic partnership that aligns well on these fronts can significantly enhance the efficiency of technology transfers. Effective collaboration minimizes delays by reducing misunderstandings and misaligned processes, allowing experienced partners to foresee and mitigate potential issues early. Such partnerships help overcome common technology transfer challenges like scale-up difficulties, formulation stability, and regulatory compliance, through the integration of complementary skills and resources.

Streamlined processes and shared resources not only lead to cost savings but also allow companies to avoid substantial investments in new equipment and personnel training. Additionally, in a sector characterized by rapidly changing market dynamics, a reliable partner is crucial for quickly adapting production strategies to meet new market demands or regulatory conditions, ensuring the company remains agile and responsive.

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A critical step forward

Technology transfer is more than a procedural necessity. It's a strategic lever in the pharmaceutical manufacturing landscape. With the industry's complex array of challenges, the role of robust, reliable technology transfer processes becomes increasingly vital. These processes ensure the consistency and quality of pharmaceutical products across various scales and locations, and they uphold the integrity and timelines of crucial drug development projects.

Companies that prioritize effective technology transfer, backed by strategic partnerships and rigorous regulatory adherence, are better positioned to adapt swiftly and efficiently to changing market demands and regulatory landscapes, enhancing their operational resilience during periods of industry uncertainty. Above and beyond strengthening competitive positioning, this can expedite the delivery of life-saving treatments to those who need them.

Additional resources:

https://www.patheon.com/us/en/insights-resources/blog/tech-transfers-for-viral-vector-commercialization.html

https://www.patheon.com/us/en/insights-resources/whitepapers/technology-transfers-best-practices-for-optimizing-successand-mitigating-risk.html

 $\underline{https://www.patheon.com/us/en/insights-resources/infographics/9-dos-and-donts-of-a-successful-technology-transfers.html}$

https://www.patheon.com/us/en/insights-resources/whitepapers/technology-transfers-reaping-rewards-reducing-risks.html

